REMARKS

Status of the Claims

Claims 1-9 and 12 and are currently pending in the application. Claims 1-12 stand rejected. Claims 7 and 12 have been amended as set forth herein. Claims 10 and 11 have been cancelled herein. All amendments and cancellations are made without prejudice or disclaimer. No new matter has been added by way of the present amendments. Specifically, the amendment to claim 7 is supported by the specification at, for instance, page 8, lines 2-8. Claim 12 has been amended to change its dependency from cancelled claim 11 to amended claim 7. Reconsideration is respectfully requested.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 10-12 stand rejected under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. (*See*, Office Action of February 9, 2007, at page 2, hereinafter "Office Action"). Claims 10 and 11 are cancelled herein without prejudice or disclaimer, thus obviating the rejection as to these claims. Applicants traverse the rejection as to claim 12 as set forth herein.

The Examiner states that the claims are indefinite for reciting amino acid homology without reciting a sequence identifier to which the homology should be compared.

The Examiner's attention is drawn to recent US legal precedent which holds that a specification need not contain a sequence listing where the specification is directed to sequences that are well known in the art. (*See*, *Faulkner v. Inglis*, 79 U.S.P.Q.2d 1001, 1008 (Fed. Cir. 2006), stating, "Indeed, the forced recitation of known sequences in patent disclosures would only

add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here 'essential genes'), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences.").

The presently claimed invention is directed to a process for producing an antibody wherein a nonhuman animal with Fas function defects is immunized with a human antigen which has homology of 90% or more at the amino acid sequence level to a homolog protein of the nonhuman animal to be immunized. Thus, the presently claimed invention is not limited to any specific protein. The Inventors herein have discovered a process by which an antibody may be produced in a mouse against a human protein which has a highly homologous protein in the genome of the mouse producing the antibody. Normally such a process presents difficulties since the mouse immune system may generate antibodies that may bind to its own proteins and be detrimental to the mouse's health. The present Inventors discovered that these types of antibodies may be produced by using MRL/lpr mice. Thus, a protein used to generate antibodies in an MRL/lpr mouse is not limited to any specific protein – it may be any protein that has a highly homologous mouse protein.

Reconsideration and withdrawal of the indefiniteness rejection of claim 12 are respectfully requested.

Rejections Under 35 U.S.C. § 102(b)

Kayagaki et al., EP 0872488

Claims 7-10 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Kayagaki et al., EP 0872488 (hereinafter referred to as "Kayagaki et al."). (*See*, Office Action, at page 2). Claim 10 has been cancelled herein without prejudice or disclaimer, thus obviating the rejection as to claim 10. Applicants traverse the rejection as to claims 7-9 as set forth herein.

The Examiner states that Kayagaki et al. disclose a method for producing an anti-Fas ligand antibody comprising immunizing an MLP/lpr mouse with Fas function defects with a Fas ligand-expressed protein as an antigen. (*Id.*).

However, amended claim 7 now recites, "A process for producing an antibody comprising immunizing a nonhuman animal with Fas function defects with a human antigen which has homology of 90% or more at the amino acid sequence level to a homolog protein of the nonhuman animal to be immunized." Thus, as amended, Kayagaki et al. fail to disclose each and every element of the presently claimed invention, especially the limitation concerning a homology of 90% or more compared to the antigen and any possible mouse homolog thereof.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." (*See, Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987)). Since Kayagaki et al. do not disclose all elements of the presently claimed invention, Kayagaki et al. do not anticipate the presently claimed invention.

Dependent claims 8 and 9 are not anticipated as, *inter alia*, depending directly or indirectly from a non-anticipated base claim, claim 7.

Reconsideration and withdrawal of the anticipation rejection of claims 7-9 are respectfully requested.

Paul et al., U.S. Patent No. 6,235,714

Claims 7-12 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Paul et al., U.S. Patent No. 6,235,714 (hereinafter referred to as "Paul et al."). (*See*, Office Action, at page 3). Claims 10 and 11 have been cancelled herein without prejudice or disclaimer, thus obviating the rejection as to claims 10 and 11. Applicants traverse the rejection as to claims 7-9 and 12 as set forth herein.

The Examiner states that Paul et al. disclose immunization of MRL/lpr mice with an antigen such as EGFR, TNFα, and IL-1β to generate catalytic antibodies. (*Id.*). The Examiner further states that the homology of these proteins between human and mouse is 90% to 94% or higher. (*Id.*).

However, amended claim 7 now recites, "A process for producing an antibody comprising immunizing a nonhuman animal with Fas function defects with a human antigen which has homology of 90% or more at the amino acid sequence level to a homolog protein of the nonhuman animal to be immunized." Thus, as amended, Paul et al. fail to disclose each and every element of the presently claimed invention, especially the limitation concerning a homology of 90% or more compared to the antigen and any possible mouse homolog thereof.

Applicants provide attached hereto as Exhibit A sequence alignment data showing the percentage homology between human and mouse EGFR, TNFα and IL-β. Applicants find that these proteins are 78%, 87% and 78% homologous, respectfully. Thus, all antigens to which

antibodies were generated in Paul et al. are lower than 90% homologous between human and mouse. Therefore, Paul et al. do not disclose all of the limitations of the presently claimed invention and cannot anticipate the presently claimed invention, especially as recited in amended claim 7.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." (*See, Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987)). Since Kayagaki et al. do not disclose all elements of the presently claimed invention, Kayagaki et al. do not anticipate the presently claimed invention.

Dependent claims 8, 9 and 12 are not anticipated as, *inter alia*, depending directly or indirectly from a non-anticipated base claim, claim 7.

Reconsideration and withdrawal of the anticipation rejection of claims 7-9 and 12 are respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Kayagaki et al. & Fu et al.

Claims 7 and 10-12 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kayagaki et al. in view of Fu et al., *Science* 297:2006-2008, 2002 (hereinafter, "Fu et al."). (*See*, Office Action, at page 3). Claims 10 and 11 have been cancelled herein without prejudice or disclaimer, thus obviating the rejection as to claims 10 and 11. Applicants traverse the rejection as to claims 7-9 and 12 as set forth herein.

The Examiner states that Kayagaki et al. do not disclose or suggest an antigen having high homology of between 90% and 94% between mouse and human. (*Id.*). However, the Examiner states that Fu et al. disclose or suggest that mice deficient in either Fas receptor or Fas ligand do not delete autoreactive B cells. (*Id.*). The Examiner further states that it would have been obvious to one of ordinary skill in the art to substitute the Fu et al. mouse to generate antibodies to highly homologous proteins according to the method of Kayagaki et al. (*Id.* at page 4).

Applicants will submit a verified English language translation of the priority document PCT/JP02/08998 following this reply. Thus, the effective filing date of the presently claimed invention of September 4, 2002 will predate the publication date of Fu et al. (September 20, 2002). Thus, Fu et al. will not be available as prior art.

Thus, as admitted by the Examiner, Kayagaki et al. do not disclose or suggest all of the limitations of the presently claimed invention. Therefore, the Examiner has failed to establish a *prima facie* case of obviousness with respect to at least amended claim 7.

Since no specific reasoning is provided for the rejection of dependent claim 12, claim 12 is also believed to be non-obvious for, *inter alia*, depending from a non-obvious base claim, amended claim 7.

Reconsideration and withdrawal of the obviousness rejection of claims 7 and 12 are respectfully requested.

Kayagaki et al., Fu et al. & Veugelers et al.

Claims 1-5 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kayagaki et al. in view of Fu et al., and further in view of Veugelers et al., *J. Biol. Chem.*, 274(38):26968-26977, 1999 (hereinafter, "Veugelers et al."). (*See*, Office Action, at page 4). Applicants traverse the rejection as set forth herein.

The Examiner states that neither Kayagaki et al. nor Fu et al. disclose or suggest the use of glypican protein as an antigen. (*Id.*). However the Examiner finds this limitation in Veugelers et al. which discloses or suggests that glypican-6 has 96% identity between mouse and human and that it would have been obvious to one of ordinary skill in the art to combine the disclosures of all three references to produce antibodies of glypican protein using Applicants' claimed methods.

However, as discussed above, Applicants will submit a verified English language translation of the priority document PCT/JP02/08998. Thus, the effective filing date of the presently claimed invention of September 4, 2002 will predate the publication date of Fu et al. (September 20, 2002).

Thus, as admitted by the Examiner, Kayagaki et al. do not disclose or suggest all of the limitations of the presently claimed invention. Therefore, the Examiner has failed to establish a *prima facie* case of obviousness with respect to independent claims 1 and 2.

Since no specific reasoning is provided for the rejection of dependent claims 3-5, claim 3-5 are also believed to be non-obvious for, *inter alia*, depending from a non-obvious base claim, claims 1 and 2.

Reconsideration and withdrawal of the obviousness rejection of claims 1-5 are respectfully requested.

Kayagaki et al., Fu et al. & Veugelers et al.

Claims 1-56 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kayagaki et al. in view of Fu et al., and further in view of Veugelers et al. (*See*, Office Action, at page 4). Applicants traverse the rejection as set forth herein.

As already discussed above, Applicants will submit a verified English language translation of the priority document PCT/JP02/08998 so that the effective filing date of the presently claimed invention will be September 4, 2002, which predates the publication date of Fu et al. (September 20, 2002).

Thus, as admitted by the Examiner, Kayagaki et al. do not disclose or suggest all of the limitations of the presently claimed invention. Therefore, the Examiner has failed to establish a *prima facie* case of obviousness with respect to independent claims 1 and 2.

Since no specific reasoning is provided for the rejection of dependent claims 3-6, claim 3-6 are also believed to be non-obvious for, *inter alia*, depending from a non-obvious base claim, claims 1 and 2.

Reconsideration and withdrawal of the obviousness rejection of claims 1-6 are respectfully requested.

CONCLUSION

If the Examiner has any questions or comments, please contact Thomas J. Siepmann, Ph.D., Registration No 57,374, at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

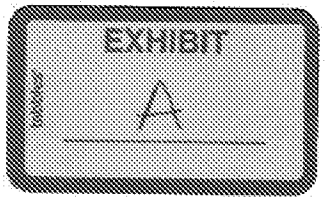
Dated: June 11, 2007 (Monday)

Respectfully submitted,

By
Gerald M. Murphy, Jr.
Registration No. 28,977
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Road
Suite 100 East
P.O. Box 747
Falls Church, Virginia 22040-0747
(703) 205-8000
Attorney for Applicants

Attachments: Exhibit A – sequence alignments of mouse and human EGFR, TNFα and IL-1β

Distance tree of results



Sequences producing significant alignments:	Score (Bits)	E Valu
ref|NP_005219.2| epidermal growth factor receptor isoform a [Hom	1286	0.0
ref|NP_958441.1| epidermal growth factor receptor isoform d [Hom	1124	0.0
ref|NP_958439.1| epidermal growth factor receptor isoform b [Hom	1122	0.0
ref|NP_958440.1| epidermal growth factor receptor isoform c [Hom	714	0.0
ref|NP_001036064.1| v-erb-a erythroblastic leukemia viral onc...	705	0.0
ref|NP_005226.1| v-erb-a erythroblastic leukemia viral oncoge...	705	0.0
ref|NP_001973.2| erbB-3 isoform 1 precursor [Homo sapiens]	639	0.0
ref|NP_004439.2| erbB-2 isoform a [Homo sapiens]	624	7e-
ref|NP_001005862.1| erbB-2 isoform b [Homo sapiens]	618	6e-
ref|NP_000199.2| insulin receptor isoform Long precursor [Homo s	119	6e-
ref|NP_001079285.1| insulin receptor isoform Short precursor [Ho	119	6e-
ref|NP_001005915.1| erbB-3 isoform s precursor [Homo sapiens]	109	1e-
ref|NP_000866.1| insulin-like growth factor 1 receptor precursor	104	2e-
ref|NP_055030.1| insulin receptor-related receptor precursor [Ho	95.9	1e-
ref|NP_612193.1| paired basic amino acid cleaving system 4 is...	52.4	1e-
ref|NP_612194.1| paired basic amino acid cleaving system 4 is...	52.4	1e-
ref|NP_612192.1| paired basic amino acid cleaving system 4 is...	51.2	3e-
ref|NP_002561.1| paired basic amino acid cleaving system 4 is...	51.2	3e-
ref|NP_006181.2| proprotein convertase subtilisin/kexin type ...	49.3	1e-
ref|NP_079350.4| Fraser syndrome 1 [Homo sapiens]	48.1	3e-
ref|NP_066363.1| zinc finger, NFXl-type containing 1 [Homo sapie	43.5	6e-
ref|NP_060445.3| Zwilch [Homo sapiens]	35.4	0.1
ref|NP_006859.2| lipoic acid synthetase isoform 1 precursor [Hom	34.7	0.3
ref|NP_056295.1| nectin 3 [Homo sapiens]	34.3	0.3
ref|NP_919433.1| lipoic acid synthetase isoform 2 precursor [Hom	34.3	0.3
ref|NP_060043.2| proprotein convertase subtilisin/kexin type 4 [	32.3	1.3
ref|NP_004186.1| tumor necrosis factor receptor superfamily, ...	31.6	2.1
ref|NP_683700.1| tumor necrosis factor receptor superfamily, ...	31.6	2.1
ref|NP_002283.3| laminin, beta 2 precursor [Homo sapiens]	31.6	2.2
ref|NP_002323.2| low density lipoprotein-related protein 1 [Homo	31.6	2.5
ref|NP_004516.2| low density lipoprotein-related protein 2 [Homo	31.2	3.1
ref|NP_683699.1| tumor necrosis factor receptor superfamily, ...	30.8	3.7
ref|NP_001035096.1| R-spondin family, member 4 isoform 2 precurs	30.4	5.4
ref|NP_009098.3| zinc finger protein 258 [Homo sapiens]	30.4	5.5
ref|NP_001026042.2| R-spondin family, member 4 isoform 1 precurs	30.4	5.7
ref|NP_055267.1| tumor necrosis factor receptor superfamily, ...	30.0	6.1
ref|XP_001131379.1| PREDICTED: similar to Fc fragment of IgG ...	30.0	6.2
ref|NP_001899.1| cathepsin B preproprotein [Homo sapiens] >re...	30.0	7.4
ref|NP_002560.1| furin preproprotein [Homo sapiens]	29.6	7.8

Alignments

>ref|NP_005219.2| EGFR epidermal growth factor receptor isoform a [Homo sapien
Length=1210

Score = 1286 bits (3328), Expect = 0.0, Method: Composition-based stats.
Identities = 627/714 (87%), Positives = 665/714 (93%), Gaps = 2/714 (0%)

```
Query  1    MRPSGTARTTLLVLLTALCAAGGALEEKKVCQGTSNRLTQLGTFEDHFLSLQRMYNNCEV  60
            MRPSGTA   LL LL ALC A  ALEEKKVCQGTSN+LTQLGTFEDHFLSLQRM+NNCEV
Sbjct  1    MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEV  60

Query  61   VLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNTVERIPLENLQIIRGNALYENTYALA  120
            VLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNTVERIPLENLQIIRGN  YEN+YALA
Sbjct  61   VLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNTVERIPLENLQIIRGNMYYENSYALA  120

Query  121  XLSNYGTNRTGLRELPMRNLQEILIGAVRFSNNPILCNMDTIQWRDIVQNVFMSNMSMDL  180
            +LSNY  N+TGL+ELPMRNLQEIL GAVRFSNNP LCN+++IQWRDIV + F+SNMSMD
Sbjct  121  VLSNYDANKTGLKELPMRNLQEILHGAVRFSNNPALCNVESIQWRDIVSSDFLSNMSMDF  180

Query  181  QSHPSSCPKCDPSCPNGSCWGGGEENCQKLTKIICAQQCSHRCRGRSPSDCCHNQCAAGC  240
            Q+H  SC KCDPSCPNGSCWG GEENCQKLTKIICAQQCS RCRG+SPSDCCHNQCAAGC
Sbjct  181  QNHLGSCQKCDPSCPNGSCWGAGEENCQKLTKIICAQQCSGRCRGKSPSDCCHNQCAAGC  240

Query  241  TGPRESDCLVCQKPQDEATCKDTCPPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYV  300
            TGPRESDCLVC+KF+DEATCKDTCPPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYV
Sbjct  241  TGPRESDCLVCRKFRDEATCKDTCPPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYV  300

Query  301  VTDHGSCVRACGPDYYEVEEDGIRKCKKCDGPCRKVCNGIGIGEFKDTLSINATNIKHFK  360
            VTDHGSCVRACG D YE+EEDG+RKCKKC+GPCRKVCNGIGIGEFKD+LSINATNIKHFK
Sbjct  301  VTDHGSCVRACGADSYEMEEDGVRKCKKCEGPCRKVCNGIGIGEFKDSLSINATNIKHFK  360

Query  361  YCTAISGDLHILPVAFKGDSFTHTPPLDPRRLEILKTVKEITGFLLIQAWPDNWTDLHAF  420
             CT+ISGDLHILPVAF+GDSFT TPPLDP+ LE++ILKTVKEITGFLLIQAWP+N TDLHAF
Sbjct  361  NCTSISGDLHILPVAFRGDSFTHTPPLDPQHLDILKTVKEITGFLLIQAWPENRTDLHAF  420

Query  421  ENLEIIRGRTKQHGQFSLAVVGLNITSLGLRSLKEISDGDVIISGNRNLCYANTINWKKL  480
            ENLEIIRGRTKQHGQFSLAVV LNITSLGLRSLKEISDGDVIISGN+NLCYANTINWKKL
Sbjct  421  ENLEIIRGRTKQHGQFSLAVVSLNITSLGLRSLKEISDGDVIISGNKNLCYANTINWKKL  480

Query  481  FGTPNQKTKIMNNRAEKDCKAVNHVCNPLCSSEGCWGPEPRDCVSCQNVSRGRECVEKCN  540
            FGT  QKTKI++NR E  CKA   VC+ LCS EGCWGPEPRDCVSC+NVSRGRECV+K N
Sbjct  481  FGTSGQKTKIISNRGENSCKATGQVCHALCSPEGCWGPEPRDCVSCRNVSRGRECVDKCN  540

Query  541  ILEGEPREFVENSECIQCHPECLPQAMNITCTGRGPDNCIQCAHYIDGPHCVKTCPAGIM  600
            +LEGEPREFVENSECIQCHPECLPQAMNITCTGRGPDNCIQCAHYIDGPHCVKTCPAG+M
Sbjct  541  LLEGEPREFVENSECIQCHPECLPQAMNITCTGRGPDNCIQCAHYIDGPHCVKTCPACVM  600

Query  601  GENNTLVWKYADANNVCHLCHANCTYGCAGPGLQGCEVWPSGPKIPSIATGIVGGLLFIV  660
            GENNTLVWKYADA +VCHLCH NCTYGC GPGL+GC     +GPKIPSIATG+VG LL  ++
Sbjct  601  GENNTLVWKYADAGKVCHLCHPNCTYGCTGPGLEGCPT--NGPKIPSIATGMVGALLLLL  658

Query  661  VVALGIGLFMRRRHIVRKRTLRRLLQERELVEPLTPSGEAPNQALLRILKETEF  714
            VVALGIGLFMRRRHIVRKRTLRRLLQERELVEPLTPSGEAPNQA LRILKETEF
Sbjct  659  VVALGIGLFMRRRHIVRKRTLRRLLQERELVEPLTPSGEAPNQALLRILKETEF  712
```

>ref|NP_958441.1| [redacted] epidermal growth factor receptor isoform d [Homo sapien
Length=705

Score = 1134 bits (2907), Expect = 0.0, Method: Composition-based stats.
Identities = 554/635 (87%), Positives = 588/635 (92%), Gaps = 0/635 (0%)

```
Query  1    MRPSGTARTTLLVLLTALCAAGGALEEKKVCQGTSNRLTQLGTFEDHFLSLQRMYNNCEV  60
            MRPSGTA   LL LL ALC A  ALEEKKVCQGTSN+LTQLGTFEDHFLSLQRM+NNCEV
Sbjct  1    MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEV  60

Query  61   VLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNTVERIPLENLQIIRGNALYENTYALA  120
            VLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNTVERIPLENLQIIRGN  YEN+YALA
Sbjct  61   VLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNTVERIPLENLQIIRGNMYYENSYALA  120

Query  121  ILSNYGTNRTGLRELPMRNLQEILIGAVRFSNNPILCNMDTIQWRDIVQNVFMSNMSMDL  180
            +LSNY  N+TGL+ELPMRNLQEIL GAVRFSNNP LCN+++IQWRDIV + F+SNMSMD
Sbjct  121  VLSNYDANATGLKELPMRNLQEILHGAVRFSNNPALQNVESIQWHDIVSSDFLSNMSMDF  180

Query  181  QSHPSSCPKCDPSCPNGSCWGGGEENCQKLTKIICAQQCSHRCRGRSPSDCCHNQCAAGC  240
            Q+H  SC KCDPSCPNGSCWG GEENCQKLTKIICAQQCS RCRG+SPSDCCHNQCAAGC
Sbjct  181  QNHLGSCQKCDPSCPNGSCWGAGEENCQKLTKIICAQQCSGRCRGKSPSDCCHNQCAAGC  240

Query  241  TGPRESDCLVCQKPQDEATCKDTCPPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYV  300
            TGPRESDCLVC+KF+DEATCKDTCPPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYV
Sbjct  241  TGPRESDCLVCRKFRDEATCKDTCPPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYV  300

Query  301  VTDHGSCVRACGPDYYEVEEDGIRKCKKCDGPCRKVCNGIGIGEFKDTLSINATNIKHFK  360
```

Distance tree of results NEW

Sequences producing significant alignments:		Score (Bits)	E Valu
ref|NP_000585.2|	tumor necrosis factor alpha [Homo sapiens]	372	1e-
ref|NP_000586.2|	lymphotoxin alpha precursor [Homo sapiens]	85.5	4e-
ref|NP_005109.2|	tumor necrosis factor (ligand) superfamily, ...	74.3	7e-
ref|NP_003798.2|	tumor necrosis factor ligand superfamily, me...	66.2	2e-
ref|NP_742011.1|	tumor necrosis factor ligand superfamily, me...	66.2	2e-
ref|NP_000630.1|	fas ligand [Homo sapiens]	57.4	9e-
ref|NP_002332.1|	lymphotoxin-beta isoform a [Homo sapiens]	56.2	2e-
ref|NP_003692.1|	tumor necrosis factor ligand superfamily, me...	52.0	4e-
ref|NP_143026.1|	tumor necrosis factor ligand superfamily, me...	52.0	4e-
ref|NP_003801.1|	tumor necrosis factor (ligand) superfamily, ...	43.5	2e-
ref|NP_000065.1|	CD40 ligand [Homo sapiens]	38.5	0.0
ref|NP_742086.1|	tumor necrosis factor (ligand) superfamily, ...	32.0	0.4
ref|NP_003799.1|	tumor necrosis factor ligand superfamily, me...	31.2	0.6
ref|NP_742084.1|	tumor necrosis factor ligand superfamily, me...	31.2	0.6
ref|NP_742085.1|	tumor necrosis factor ligand superfamily, me...	31.2	0.6
ref|NP_006564.1|	tumor necrosis factor (ligand) superfamily, ...	31.2	0.6
ref|NP_001235.1|	tumor necrosis factor (ligand) superfamily, ...	29.3	2.9
ref|NP_001003398.1|	bicaudal D homolog 1 isoform 2 [Homo sapiens	27.7	7.2
ref|NP_001705.2|	bicaudal D homolog 1 isoform 1 [Homo sapiens]	27.7	8.8
ref|NP_054836.2|	hypothetical protein LOC29035 [Homo sapiens]	27.3	9.3

Alignments

>ref|NP_000585.2| UG tumor necrosis factor alpha [Homo sapiens]
Length=233

Score = 372 bits (956), Expect = 1e-103, Method: Composition-based stats.
Identities = 186/236 (78%), Positives = 211/236 (89%), Gaps = 4/236 (1%)

```
Query  1    MSTESMIRDVELAEEALPQKMGGFQNSRRCLCLSLFSFLLVAGATTLFCLLNFGVIGPQR  60
            MSTESMIRDVELAEEALP+K GG Q SRRCL LSLFSFL+VAGATTLFCLL+FGVIGPQR
Sbjct  1    MSTESMIRDVELAEEALPKKTGGPQGSRRCLFLSLFSFLIVAGATTLFCLLHFGVIGPQR  60

Query  61   DEKQFPNGLPLISSMAQTLTLRSSSQNSSDKPVAHVVANHQVEEQLEWLSQRANALLANGM  120
            +E FP  L LIS +AQ +  RSSS+  SDKPVAHVVAN Q E QL+WL++RANALLANG+
Sbjct  61   EE-FPRDLSLISFLAQAV--RSSSETPSDKPVAHVVANPQAEGQLQWLNRRANALLANGV  117

Query  121  DLKDNQLVVPADGLYLVYSQVLFKGQGCPD-YVLLTHTVSRFAISYQEKVNLLSAVKSPC  179
            +L+DNQLVVP++GLYL+YSQVLFKGQGCP  +VLLTHT+SR A+SYQ KVNLLSA+KSPC
Sbjct  118  ELRDNQLVVPSEGLYLIYSQVLFKGQGCPSTHVLLTHTISRIAVSYQTKVNLLSAIKSPC  177

Query  180  PKDTPEGAELKPWYEPIYLGGVFQLEKGDQLSAEVNLPKYLDFAESGQVYFGVIAL  235
             ++TPEGAE KPWYEPIYLGGVFQLEKGD+LSAE+N P YLDFAESGQVYFG+IAL
Sbjct  178  QRETPEGAEAKPWYEPIYLGGVFQLEKGDRLSAEINRPDYLDFAESGQVYFGIIAL  233
```

>ref|NP_000586.2| UG lymphotoxin alpha precursor [Homo sapiens]
Length=205

Score = 85.5 bits (210), Expect = 4e-17, Method: Composition-based stats.
Identities = 61/176 (34%), Positives = 86/176 (48%), Gaps = 14/176 (7%)

```
Query  67   GLPLISSMAQTLTLRSSSQ--NSSDKPVAHVVANHQVEEQLEWLSQRANALLANGMDLKD  124
            G+ L  S AQT          +S+ KP AH++ +   + L W +    A L +G  L +
Sbjct  37   GVGLTPSAAQTARQHPKMHLAHSTLKPAAHLIGDPSKQNSLLWRANTDRAFLQDGFSLSN  96
```

Distance tree of results

Sequences producing significant alignments:		Score (Bits)	E Valu
ref|NP_000567.1|	interleukin 1, beta proprotein [Homo sapiens]	232	9e-
ref|NP_775270.1|	interleukin 1 family, member 8 isoform 2 [Homo	59.7	7e-
ref|NP_776214.1|	interleukin 1 receptor antagonist isoform 1 ...	58.9	2e-
ref|NP_000568.1|	interleukin 1 receptor antagonist isoform 3 [Ho	58.2	3e-
ref|NP_776215.1|	interleukin 1 receptor antagonist isoform 4 [Ho	58.2	3e-
ref|NP_776213.1|	interleukin 1 receptor antagonist isoform 2 [Ho	58.2	3e-
ref|NP_115948.4|	interleukin 1 family, member 10 [Homo sapien...	51.6	2e-
ref|NP_036407.1|	interleukin 1 family, member 5 [Homo sapiens...	47.8	4e-
ref|NP_062564.1|	interleukin 1 family, member 9 [Homo sapiens]	40.8	4e-
ref|NP_775295.1|	interleukin 1 family, member 7 isoform 3 [Homo	36.6	0.0
ref|NP_775296.1|	interleukin 1 family, member 7 isoform 4 [Homo	36.6	0.0
ref|NP_775294.1|	interleukin 1 family, member 7 isoform 2 [Homo	36.2	0.0
ref|NP_775297.1|	interleukin 1 family, member 7 isoform 5 [Homo	36.2	0.0
ref|NP_055254.2|	interleukin 1 family, member 7 isoform 1 pro...	35.8	0.0
ref|NP_055255.1|	interleukin 1 family, member 6 (epsilon) [Homo	35.8	0.0
ref|NP_055253.2|	interleukin 1 family, member 8 isoform 1 [Homo	32.0	0.1
ref|NP_000566.3|	interleukin 1, alpha proprotein [Homo sapiens]	29.6	0.6
ref|NP_036243.1|	AHA1, activator of heat shock 90kDa protein ...	28.6	0.9
ref|NP_005056.3|	cal-1 suppressor of lin-12-like [Homo sapiens]	28.9	1.6
ref|NP_000227.1|	lipase C precursor [Homo sapiens]	28.5	2.1
ref|NP_000452.2|	thyroid hormone receptor, beta [Homo sapiens]	27.3	4.7
ref|NP_000606.3|	neural cell adhesion molecule 1 isoform 1 [Homo	26.6	8.1
ref|NP_851996.2|	neural cell adhesion molecule 1 isoform 2 [Homo	26.6	8.9

Alignments

>ref|NP_000567.1| Hide interleukin 1, beta proprotein [Homo sapiens]
Length=269

Score = 232 bits (591), Expect = 9e-62, Method: Compositional matrix adjust.
Identities = 119/152 (78%), Positives = 132/152 (86%), Gaps = 1/152 (0%)

```
Query  2    PIRQLHYRLRDEQQKSLVLSDPYELKALHLNGQNINQQVIFSMSFVQGEPSNDKIPVALG  61
            P+R L+  LRD QQKSLV+S PYELKALHL GQ++ QQV+FSMSFVQGE SNDKIPVALG
Sbjct  118  PVRSLNCTLRDSQQKSLVMSGPYELKALHLQGQDMEQQVVFSMSFVQGEESNDKIPVALG  177

Query  62   LKGKNLYLSCVMKDGTPTLQLESVDPKQYPKKKMEKRFVFNKIEVKSKVEFESAEFPNWY  121
            LK KNLYLSCV+KD  PTLQLESVDPK YPKKKMEKRFVFNKIE+ +K+EFESA+FPNWY
Sbjct  178  LKEKNLYLSCVLKDDKPTLQLESVDPKNYPKKKMEKRFVFNKIEINNKLEFESAQFPNWY  237

Query  122  ISTSQAENMPVFL-GNNSGQDIIDFTMESVSS  152
            ISTSQAE+ PVFL G   GQDI DFTM+ VSS
Sbjct  238  ISTSQAEHKPVFLGGTKGGQDITDFTMQFVSS  269
```

>ref|NP_775270.1| Hide interleukin 1 family, member 8 isoform 2 [Homo sapiens]
Length=157

Score = 59.7 bits (143), Expect = 7e-10, Method: Compositional matrix adjust.
Identities = 36/95 (37%), Positives = 54/95 (56%), Gaps = 2/95 (2%)

```
Query  58   VALGLKGKNLYLSCVMKDGTPTLQLESVDPKQ-YPKKKMEKRFVFNKIEVKSKVEFESAE  116
            V LG+KGK+L L C     G PTLQL+  +     Y +KK +K P+F   +  S   F+S
Sbjct  62   VVLGIKGKDLCLFCAEIQGKPTLQLKEKNIMDLYVEKKAQKPFLFFHNKEGSTSVFQSVS  121
```